

Oxygenated Fuels and Conventional Gasoline Health Testing Performed under the Clean Air Act Section 211

<http://www.epa.gov/OMSWWW/fuels.htm>

Presentation for : Blue Ribbon Panel to Review the Use of Oxygenates in Gasoline

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Fuel/Fuel Additive Health Testing Rule finalized in May, 1994

Purpose:

- To determine the potential adverse health effects of fuel and fuel additive (F/FA) exhaust and evaporative emissions.
 - Evaluate the effects of inhalation exposure to the whole complex emission mixtures
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Who is affected?

- Manufacturers of gasoline and diesel fuels and additives for on-road use -- designed for highways and city streets.
 - Both existing and new fuel additives.
 - For new fuels and additives, testing must be completed before introduction into commerce.
 - For existing fuels and additives, testing must be performed to retain registration (license to introduce)
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Who does the testing?

- Rule provides for voluntary grouping and cost sharing.
- e.g. American Petroleum Institute (API)-sponsored consortium is working on baseline gasoline, oxygenated gasolines (several types including MTBE) and diesel fuel.
- Besides MTBE, oxygenates being studied include tertiary butyl alcohol (TBA), tertiary amyl methyl ether (TAME), ethyl tertiary butyl ether (ETBE), ethanol, and diisopropyl ether (DIPE)

Tier 1 Literature search and emissions speciation

- Literature search on health/welfare effects of emissions
 - Emissions characterization and measurement of hydrocarbon species such as ketones, aldehydes, alcohols, ethers, PAHs, NPAHs and “atypical emissions as applicable.
 - Tier 1 has already been submitted in most cases
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Standard Tier 2 Short-term toxicology testing

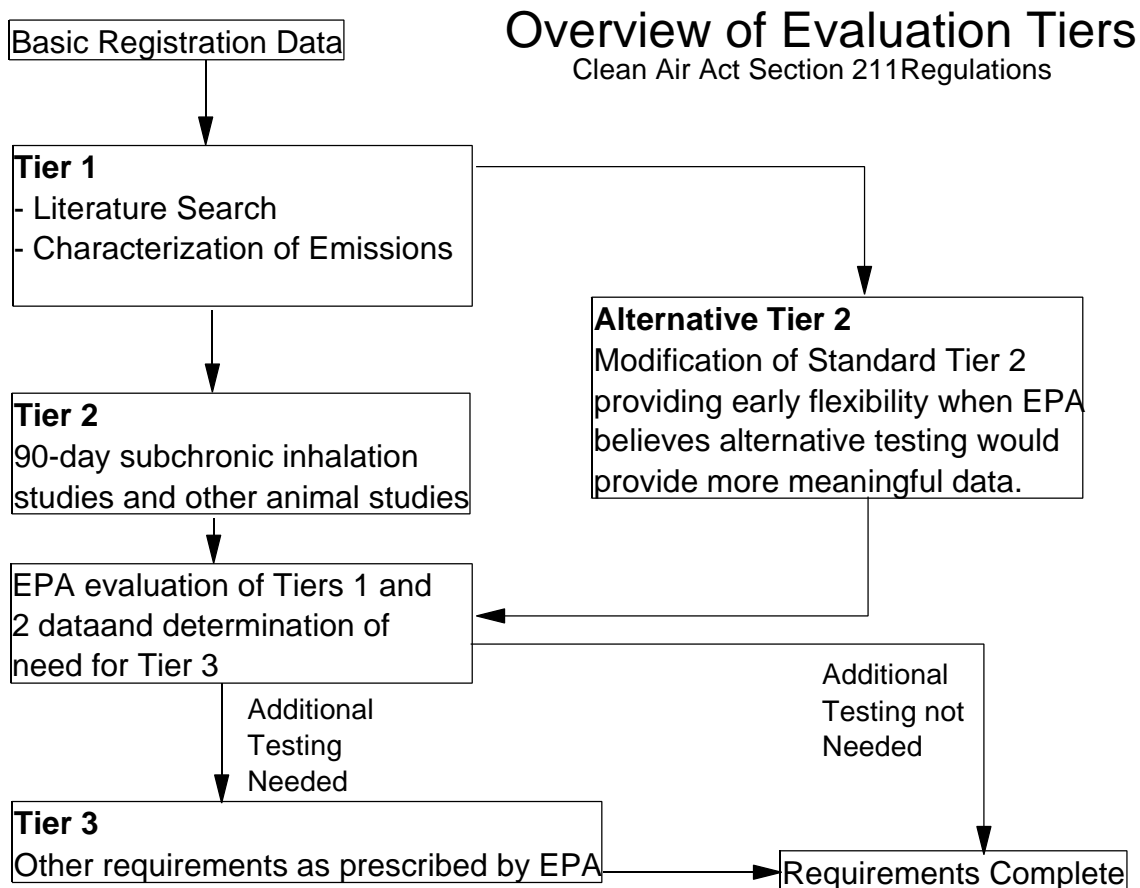
- Short-term toxicology testing generally consisting of 90-day subchronic inhalation exposures
 - Animals exposed to real-time vehicle emissions
 - Evaluation of general organ/systemic toxicity
 - Endpoints: - carcinogenicity and mutagenicity
 - developmental and fertility effects
 - pulmonary effects
 - neurotoxic effects
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Tier 3 Follow-up testing (if needed) on case-by-case basis

- Targeted to specific concerns
- High degree of discretion based on previous data

Alternative Tier 2

- EPA has authority to modify standard Tier 2
- This can be used when alternative testing may prove more valuable.
- Most testing will be performed under this provision.



Oxygenate Issues

- Regulations define a separate group for each oxygenate when oxygenate is used at significant level (i.e., not at very low traditional additive level.)
- e.g., In gasoline groups there are separate groups for TBA, MTBE, ethanol, etc.
- Because of specifically identified data gaps, EPA has decided to specify expanded Alternative Tier 2 testing for Baseline Gasoline and Oxygenated Gasoline

Baseline Gasoline and Oxygenated Gasoline

- Notification finalized on November 2, 1998 after public comment period.
- Standard testing:
 - 90-day inhalation toxicity study
 - Fertility/teratogenicity
 - Neurotoxicity
 - Carcinogenicity
 - Mutagenicity

Alternative Tier 2 Requirements for Oxyfuels

Objectives

- Extensive characterization of evaporative emissions toxicity for:

Baseline gasoline

MTBE-gasoline

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- Screening level characterization of evaporative emissions toxicity for:

ETBE-gasoline

TAME-gasoline

DIPE-gasoline

EtOH-gasoline

TBA-gasoline

F/FA Rule: Oxyfuels

"Baseline" gasoline ($<1.5\%$ -wt O_2)

"Nonbaseline" gasoline ($\geq 1.5\%$ -wt O_2):

- MTBE - 15%-vol
- ETBE - 17%-vol
- TAME - 17%-vol
- DIPE - 17%-vol
- EtOH - 10%-vol
- TBA - 12%-vol

Oxyfuel Testing Requirements

	<u>Baseline & MTBE-gasoline</u>	<u>Other oxyfuels</u>
90-day inh. toxicity	Std.	Std.
Reproductive	2-generation	Std.
Developmental	2-species	Std.
Neurotoxicity	Std. plus FOB, Motor Activity	Std.
Carcinogenicity	2-year bioassay	Std.
Immunotoxicity	SRBC	SRBC
PKs (neat vapors)	--	A-D-M-E

- Exposure Testing: Information related to human exposure levels of chemicals from evaporative and combustion emissions of MTBE oxyfuels and conventional gasoline including:

Personal exposure monitoring in various microenvironments

Ambient air measurements under various climate conditions.

Exposure measured include emissions products of these fuels as well as transformation products.

Contingent Studies (Tier 3)

- Follow-up to Alternative or Standard Tier 2
- Combustion emissions
- Acute health effects
- Atmospheric transformation products
- Change in oxygenate usage
- Other information

Rationale for Oxyfuels Testing Requirements

- Focus on fuels with greatest exposure
 - Fill in database for baseline and MTBE-gasoline
 - Obtain basic toxicity and PK information for other oxyfuels
 - Follow up as appropriate
 - Defer combustion emissions testing; obtain exposure data
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Procedural Issues Associated with 211 Testing

- Non-standardized protocols will be peer reviewed and submitted to EPA for approval
 - All results will be peer reviewed and submitted to EPA
 - Final reports on health testing are due to be submitted over a period ranging from May, 2001 through July, 2003.
 - Final report on exposure testing due to be submitted by November, 2002.
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Testing is also being conducted on other gasoline/diesel groups.

- The API consortium has already submitted sufficient data for Tier 2 requirements on typical (baseline) diesel fuel.
- The biodiesel industry is performing research on biodiesel fuel, an oxygenated diesel fuel made by chemically combining alcohol and vegetable or animal-derived oil producing an ester.
- Testing will be done on manganese-containing additives and may be done on diesel fuels containing some atypical elements (elements other than C, H, O, N, or S).
- Results will be reported over the next several years.

More Detailed Descriptions of Standard Testing

Ninety-day Inhalation Toxicity Study

- 30 rodents per concentration per group
Add specified numbers for combined assessments
Recovery group (N = 20)
- Observation
- Clinical exams:
Hematology
Clinical biochemistry
- Ophthalmological exam
- Urinalysis
- Gross pathology
- Histopathology (esp. respiratory tract)

Fertility/Teratology

- 25 males, 40 females per group, mating after 9 weeks of exposure, then females exposed through GD 15
- Limit test, observation for ≤ 13 weeks
- Vaginal cytology
- Mating and fertility
- Gross necropsy (esp. reproductive organs)
- Fetal anomalies, resorptions
- Histopathology of reproductive organs

Neuropathology

- N = 10 per group; N = 20 for recovery group
- Positive control
- Limit test
- Observation
- Brain size and weight; LM (and possible EM)
- Peripheral nerve teasing

Glial Fibrillary Acidic Protein

- 10 animals per group
- Change in amount of GFAP for specific brain region as a function of treatment and dose

In Vivo Micronucleus

- 5 females, 5 males per group
- Positive control

In-Vivo Sister Chromatid Exchange

- 5 females, 5 males per group
- Positive control

***Salmonella Typhimurium* Reverse Mutation**

- Positive control
- Data presented as number of revertant colonies per late, per kilogram (or liter) of fuel, and per kilometer (or mile) for each replicate and dose